CLAIMS

We claim:

1. A flow electroporation device, comprising:

walls defining a flow channel configured to receive and to transiently contain a continuous flow of a suspension comprising particles;

an inlet flow portal in fluid communication with the flow channel, whereby the suspension can be introduced into the flow channel through the inlet flow portal;

an outlet flow portal in fluid communication with the flow channel, whereby the suspension can be withdrawn from the flow channel through the outlet flow portal;

the walls defining the flow channel comprising a first electrode plate forming a first wall of the flow channel and a second electrode plate forming a second wall of the flow channel opposite the first wall; wherein the area of the electrodes contact with the suspension, and the distance between the electrodes is chosen so that the thermal resistance of the flow channel is less than approximately 4°C per Watt.

the paired electrodes placed in electrical communication with a source of electrical energy, whereby an electrical field is formed between the electrodes;

whereby the suspension of the particles flowing through the flow channel can be subjected to an electrical field formed between the electrodes.

2. The flow electroporation device of Claim 1, wherein the electrode plates defining the flow channel further comprises: a gasket formed from an electrically non-conductive material and disposed between the first and second electrode plates to maintain the electrode plates in spaced-apart relation, the gasket defining a channel therein forming opposed side walls of the flow channel.

3. The flow electroporation device of Claim 2, wherein the gasket forms a seal with each of the first and second electrode plates.

4. The flow electroporation device of Claim 1, wherein the device comprises a plurality of flow channels, and wherein the gasket comprises a plurality of channels forming opposed side walls of each of the plurality of channels.

5. The flow electroporation device of Claim 1, wherein one of the inlet flow portal and the outlet flow portal comprises a bore formed in one of the electrode plates and in fluid communication with the flow channel.

6. The flow electroporation device of Claim 5, wherein the other of the inlet flow portal and the outlet flow portal comprises a bore formed in the one of the electrode plates and in fluid communication with the flow channel.

7. The flow electroporation device of Claim 5, wherein the other of the inlet flow portal and the outlet flow portal comprises a bore formed in the other of the electrode plates and in fluid communication with the flow channel.

8. The flow electroporation device of Claim 1, further comprising a cooling element operatively associated with the flow channel to dissipate heat.

9. The flow electroporation device of Claim 8, wherein the cooling element comprises a thermoelectric cooling element.

10. The flow electroporation device of Claim 8, wherein the cooling element comprises a cooling fluid flowing in contact with the electrode.

11. The flow electroporation device of Claim 1, wherein the cooling element comprises a heat sink operatively associated with the electrode.

12. The flow electroporation deivice of Claim 1, wherein the resistance of the flow channel is less than approximately 3°C per watt.

13. The flow electroporation deivice of Claim 1, wherein the resistance of the flow channel is less than approximately 2°C per watt.

14. The flow electroporation device of Claim 1, wherein the resistance of the flow channel is between approximately 0.5 °C per Watt and 4°C per Watt.

15. The flow electroporation device of Claim 1, wherein the resistance of the flow channel is between approximately 1°C per Watt and 3°C per Watt.

16. The flow electroporation device of Claim 1, wherein the resistance of the flow channel is between approximately 1.5°C and 2.5°C.

17. The flow electroporation device of Claim 1, wherein the first electrode comprises an elongated, electrically conductive structure,

wherein the second electrode comprises a tubular, electrically conductive structure;

wherein the electrodes are concentrically arranged such that the second, tubular electrode surrounds the first electrode in spaced-apart relation thereto; and

wherein the flow channel is disposed within an annular space defined between the first and second electrodes.

18. The flow electroporation device of Claim 17, wherein the electrodes form at least a portion of the walls defining the flow channel.

19. The flow electroporation device of Claim 17, further comprising concentric annular spacers for maintaining the first and second electrodes in spaced-apart, concentric relation.

20. The flow electroporation device of Claim 17, wherein the device is arranged in series with a second, like device.

21. The flow electroporation device of Claim 17, wherein the device is arranged in parallel with a second, like device.

22. A method of transfecting a cell comprising providing an expression vector coding for a desired protein or peptide and introducing the expression vector into the cell by flow electroporation.

23. The method of Claim 22 wherein between approximately 50% and 95% of the cells transfected by electroporation express the desired protein.

24. The method of Claim 23, wherein between approximately 60% and 90% of the cells transfected by electroporation express the desired protein.

25. The method of Claim 24, wherein between approximately 70% and 80% of the cells transfected by flow electroporation express the desired protein.

26. The method of Claim 22, wherein the cells transfected by flow electroporation are between approximately 50% and 90% viable.

27. The method of Claim 22, wherein the cells transfected by flow electroporation art between approximately 60% and 90% viable.

28. The method of Claim 22, wherein the cells transfected by flow electroporation art between approximately 70% and 80% viable.

29. The method of Claim 22, where and the desired protein is b-cell differentiation factor, b-cell growth factor, mitogenic cytokine, chemotactic cytokine, colony stimulating factor, angiogenesis factor, cadherin, selectin, inteegrin, NCAM, ICAM, L1, t-cell replacing factors, differentiation factor, transcription factor, mRNA, heat shock protein, nuclear protein complexe, RNA/DNA oligomer, IFN-alpha, IFN-beta, IFN-omega, IL1, IL2, IL3, IL4, IL5, IL6, IL7, IL8, IL9,

IL10, IL11, IL12, IL13, IL14, IL15, IL16, IL17, IL18, leptin, myostatin, macrophage stimulating protein, platelet-derived growth factor, TNF-alpha, TNF-beta, NGF, CD40L, CD137L/4-1BBL, human lymphotoxin-beta, TNF-related apoptosis-inducing ligand, monoclonal antibody, fragments of monoclonal antibody, G-CSF, M-CSF, GM-CSF, PDGF, IL1-alpha, IL1-beta, FGF IFN-gamma, IP-10, PF4, GRO, 9E3, erythropoietin, endostatin, angiostatin, fibroblast growth factor. VEGF, or soluble receptor and any fragments or combinations thereof.

30. The method of Claim 29, wherein the desired protein is erythropoietin or fragments thereof.

31. The method of Claim 29, wherein the desired protein is endostatin or fragments thereof.

32. The method of Claim 29, wherein the desired protein is angiostatin or fragments thereof.

33. The method of Claim 29, wherein the desired protein is IL12 or fragments thereof.

34. The method of Claim 29, wherein the desired protein is IL2 or fragments thereof.

35. A method of delivering a therapeutic agent to patient comprising:

incorporating the therapeutic agent into platelets by electroporation;

administering the platelets to the patient.

36. The method of Claim 35, wherein the electroporation is flow electroporation.

37. The method of Claim 35, wherein the platlets are administered to the patient intravenously.

38. The method of claim 35, wherein the therapeutic agent is AGM-1470 (TNP-470), MetAP-2; growth factor antagonists, antibodies to growth factors; growth factor receptor antagonists; TIMP, batimastat, marimastat; genistein SU5416; alphaVbeta3/5, retinoic acid fenretinide, 11$\tilde{\alpha}$epihydrocortisol, corteloxone, tetrahydrocortisone and 17α-hydroxyprogesterone; staurosporine, MDL 27032; vitamin D derivatives including 22-oxa-1 alpha, and 25-dihydroxyvitamin D3; arachidonic acid inhibitors including indomethacin and sulindac; tetracycline derivatives including minocycline; thalidomide derivatives; 2-methoxyestradiol; tumor necrosis factor-alpha; interferon-gamma-inducible protein 10 (IP-10); interleukin 1 and interleukin 12; interferon alpha, beta or gamma; angiostatin protein or plasminogen fragments; endostatin protein or collagen 18 fragments; proliferin-related protein; group B streptococcus toxin; CM101; CAI; troponin I; squalamine; nitric

oxide synthase inhibitors including L-NAME; thrombospondin; wortmannin; amiloride; spironolactone; ursodeoxycholic acid; bufalin; suramin; tecogalan sodium; linoleic acid; captopril; irsogladine; FR-118487; triterpene acids; castanospermine; leukemia inhibitory factor; lavendustin A; platelet factor-4; herbimycin A; diaminoantraquinone; taxol; aurintricarboxylic acid; DS-4152; pentosan polysulphite; radicicol; fragments of human prolactin; erbstatin; eponemycin; shark cartilage; protamine; Louisianin A, C and D; PAF antagonist WEB 2086; auranofin; ascorbic ethers; or sulfated polysaccharide D 4152.

39. A method of treating a patient with a therapeutic protein comprising:

transfecting a cell population with an expression vector that codes for the desired protein by flow electroporation;

administering the transfected cell to the patient.

40. The method of Claim 39, wherein the therapeutic protein is b-cell differentiation factor, b-cell growth factor, mitogenic cytokine, chemotactic cytokine, colony stimulating factor, angiogenesis factor, cadherin, selectin, inteegrin, NCAM, ICAM, L1, t-cell replacing factors, differentiation factor, transcription factor, mRNA, heat shock protein, nuclear protein complexe, RNA/DNA oligomer, IFN-alpha, IFN-beta, IFN-omega, IL1, IL2, IL3, IL4, IL5, IL6, IL7, IL8, IL9, IL10, IL11, IL12, IL13, IL14, IL15, IL16, IL17, IL18, leptin, myostatin, macrophage stimulating protein, platelet-derived growth factor, TNF-alpha, TNF-beta, NGF, CD40L,

CD137L/4-1BBL, human lymphotoxin-beta, TNF-related apoptosis-inducing ligand, monoclonal antibody, fragments of monoclonal antibody, G-CSF, M-CSF, GM-CSF, PDGF, IL1-alpha, IL1-beta, FGF IFN-gamma, IP-10, PF4, GRO, 9E3, erythropoietin, endostatin, angiostatin, fibroblast growth factor. VEGF, or soluble receptor and any fragments or combinations thereof.

41. The method of Claim 39, wherein the desired protein is erythropoietin or fragments thereof.

42. The method of Claim 39, wherein the desired protein is endostatin or fragments thereof.

43. The method of Claim 39, wherein the desired protein is angiostatin or fragments thereof.

44. The method of Claim 39, wherein the desired protein is IL12 or fragments thereof.

45. The method of Claim 39, wherein the desired protein is IL2 or fragments thereof.